

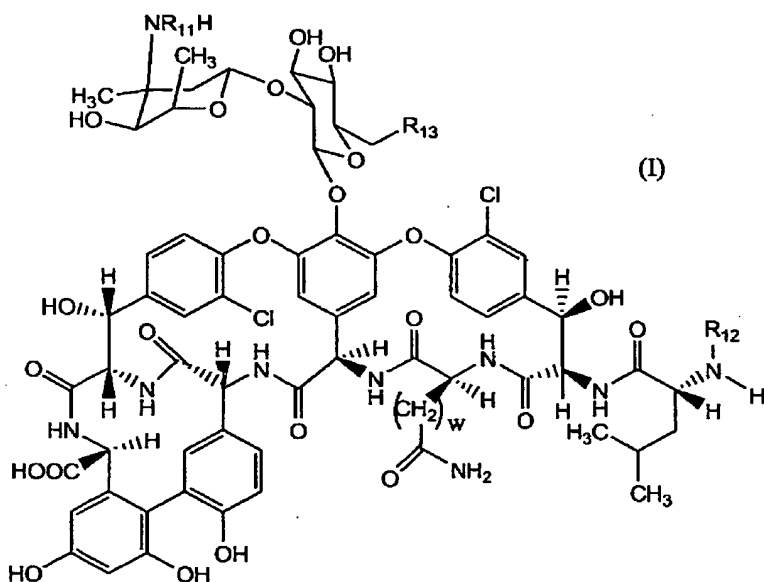
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**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1. (Original) A method of preparing a vancomycin-polymer conjugate, comprising:  
reacting a vancomycin compound of the formula:



wherein

$R_{11}$  and  $R_{12}$  are independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  heteroalkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxyalkyl, phenoxyalkyl and  $C_{1-6}$  heteroalkoxys;

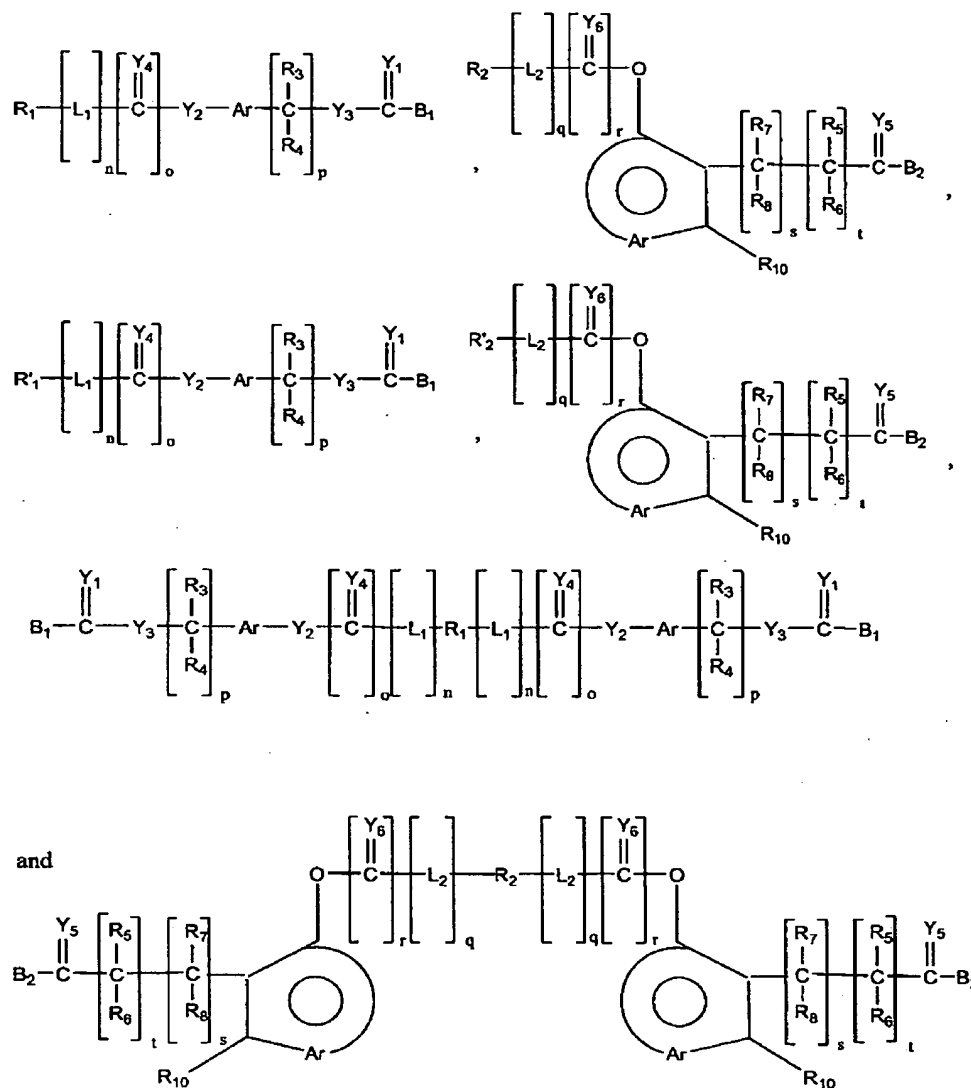
$R_{13}$  is OH, NH-aryl, NH-aralkyl, or NH- $C_{1-12}$  alkyl; and

w is 1 or 2;

with a polymer residue containing at least one leaving group capable of reacting with the sugar amino group of said vancomycin compound in the presence of at least about a ten-fold molar excess of triethylamine and a sufficient amount of dimethylformamide.

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2. (Original) The method of claim 1, wherein said activated polymer residue is selected from the group consisting of:



wherein:

$R_1$  and  $R_2$  are independently selected polymer residues;

$Y_{1-6}$  are independently selected from the group consisting of O, S or  $NR_9$ ;

$R_{3-10}$  are independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls,

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substituted aryls, aralkyls, C<sub>1-6</sub> heteroalkyls, substituted C<sub>1-6</sub> heteroalkyls, C<sub>1-6</sub> alkoxyalkyl, phenoxyalkyl and C<sub>1-6</sub> hetero-alkoxys;

Ar is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

L<sub>1</sub> and L<sub>2</sub> are independently selected bifunctional linkers;

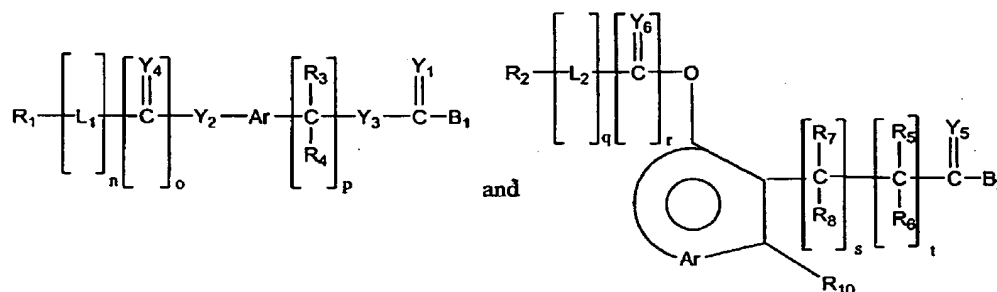
B<sub>1</sub> and B<sub>2</sub> are independently selected leaving groups;

p and t are independently selected positive integers;

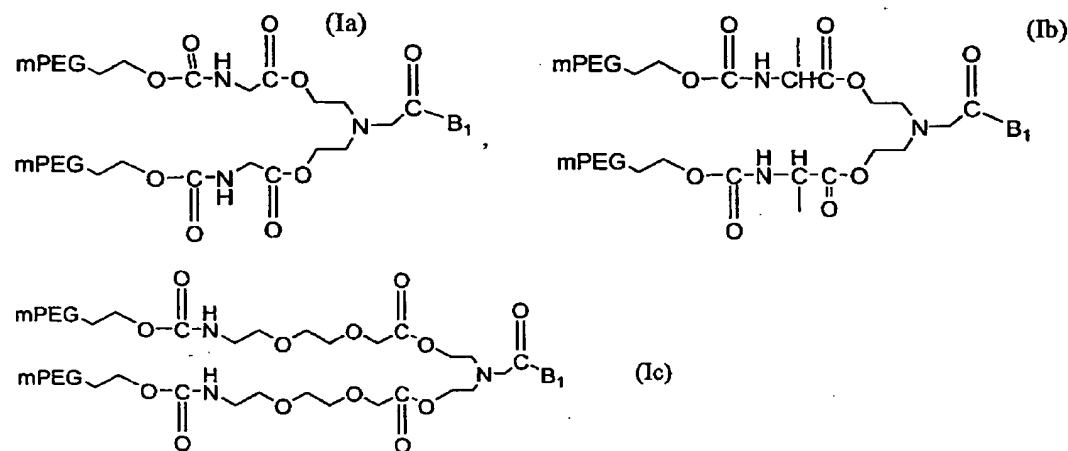
n, q and s are independently either zero or a positive integer; and

o and r are independently zero or one.

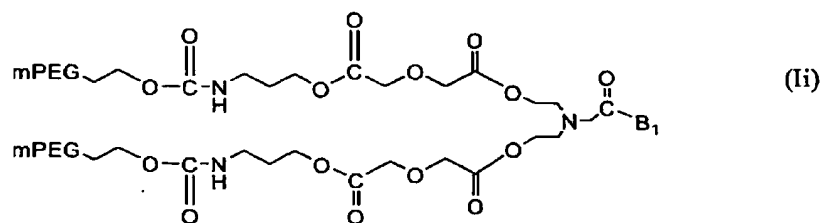
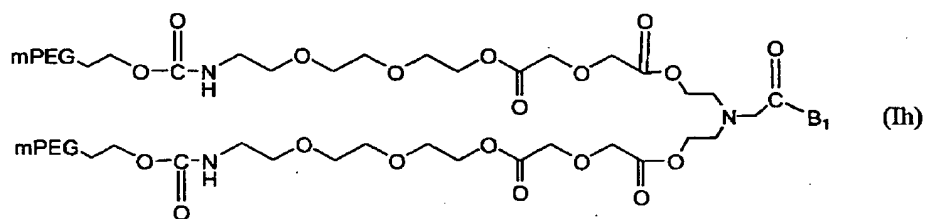
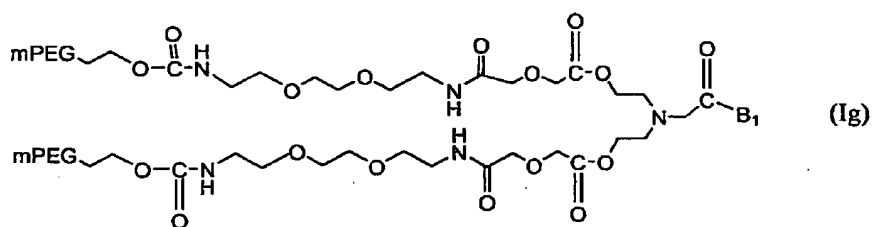
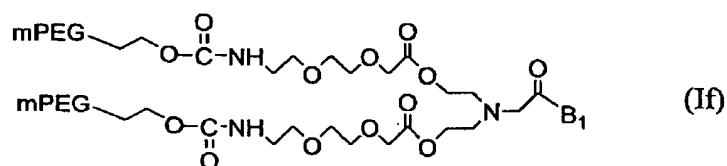
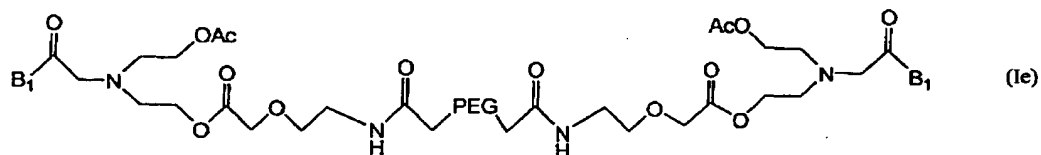
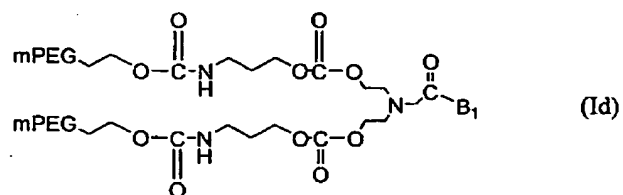
3. (Original) The method of claim 2, wherein said activated polymer residue is selected from the group consisting of



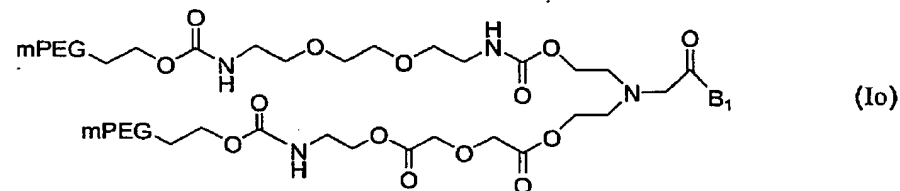
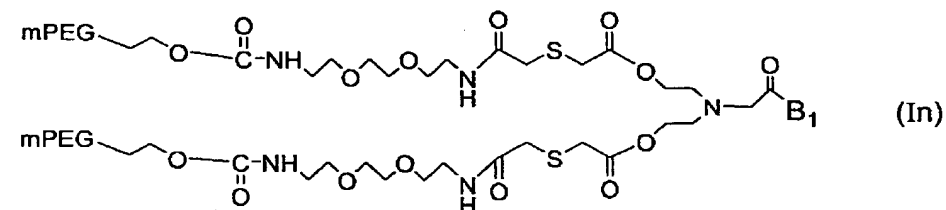
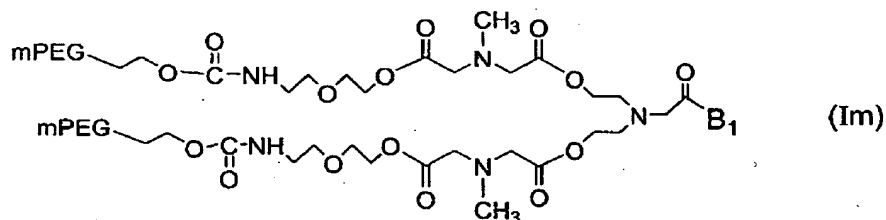
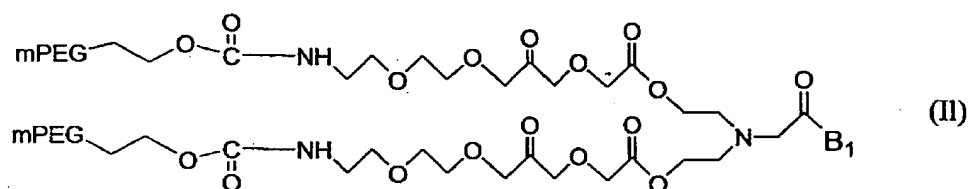
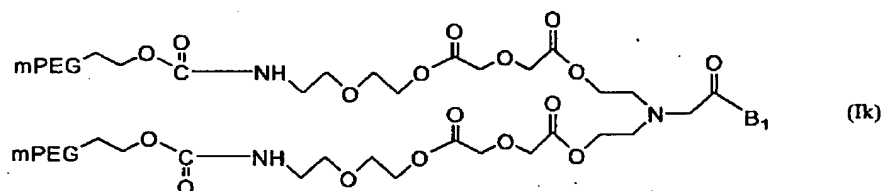
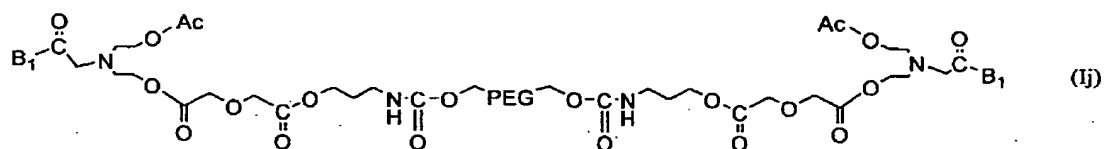
4. (Original) The method of claim 1, wherein said activated polymer residue is selected from the group consisting of:



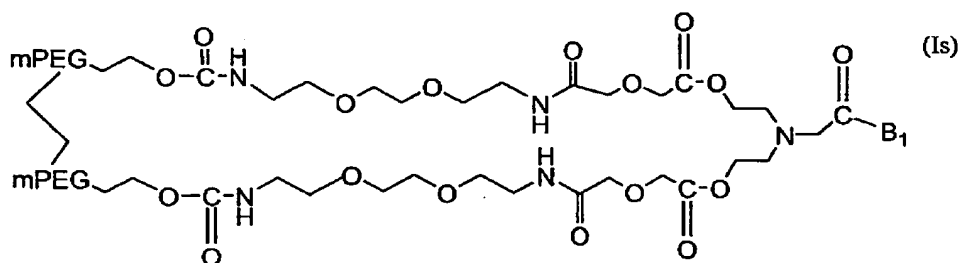
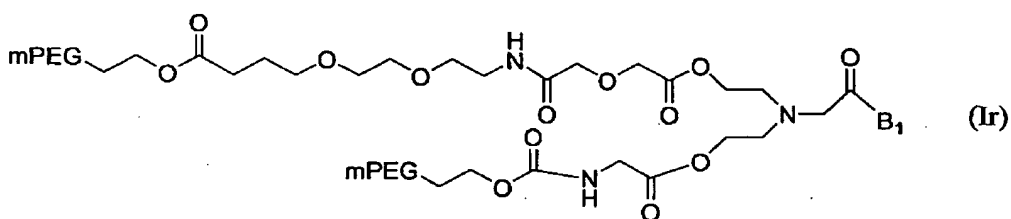
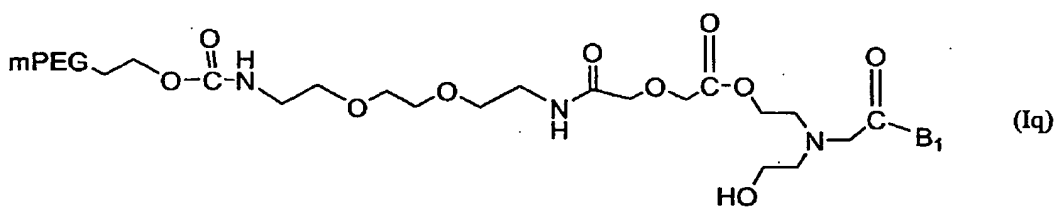
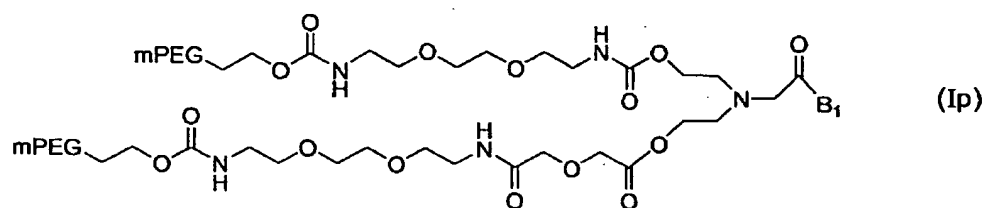
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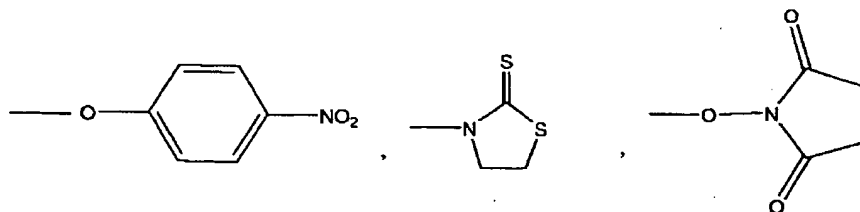
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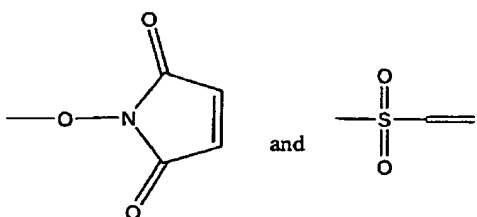
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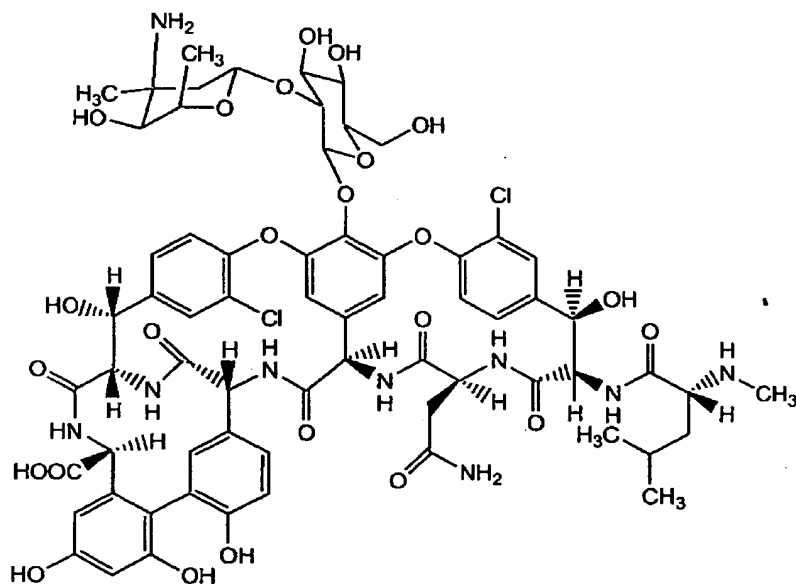
wherein B<sub>1</sub> is selected from the group consisting of:



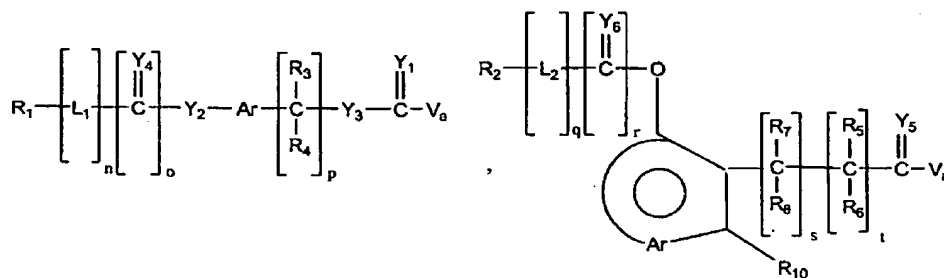
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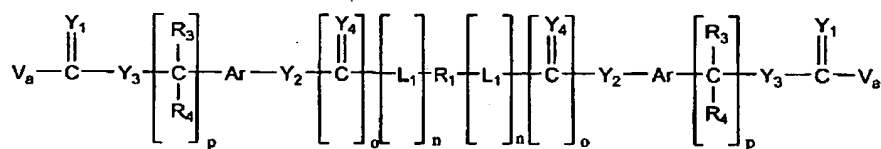


5. (Original) The method of claim 1, wherein said vancomycin compound is:



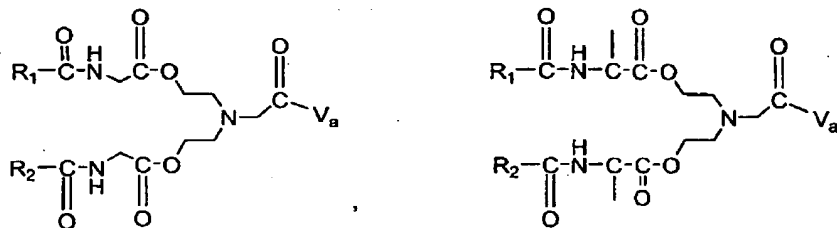
6. (Original) The method of claim 2, wherein said vancomycin polymer conjugate is selected from the group consisting of



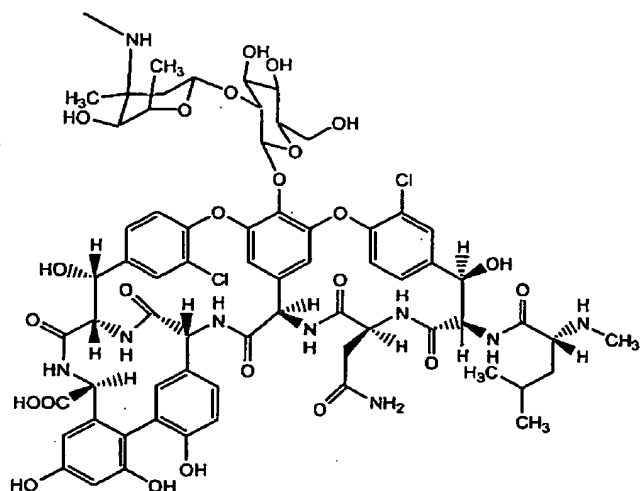
$$\begin{array}{c} R'_1 - \left[ L_1 - C \right]_n - \left[ \begin{array}{c} Y_4 \\ || \\ C \end{array} \right]_o - Y_2 - Ar - \left[ \begin{array}{c} R_3 \\ | \\ C \\ | \\ R_4 \end{array} \right]_p - Y_3 - C(Y_1) = V_8 \end{array}$$
  
$$R'_2 - \left[ L_2 - C \right]_q - \left[ \begin{array}{c} Y_6 \\ || \\ C \end{array} \right]_r - O - \text{Cyclohexyl} - \left[ \begin{array}{c} R_7 \\ | \\ C \\ | \\ R_8 \end{array} \right]_s - \left[ \begin{array}{c} R_5 \\ | \\ C \\ | \\ R_6 \end{array} \right]_t - C(Y_5) = V_a$$


and

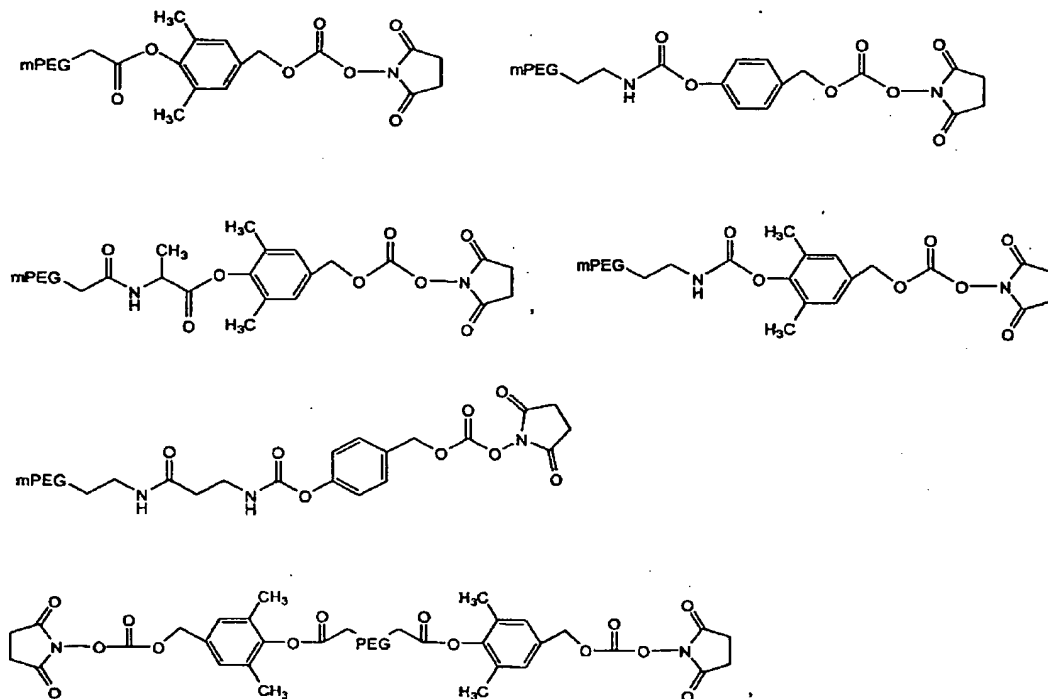
The structure shows a copolymer with two aromatic rings (Ar) connected by a central chain. The left aromatic ring is substituted with a group  $R_{10}$  and a side chain  $-C(=Y_5)-[C(R_5)(R_6)]_t-[C(R_7)(R_8)]_s-$ . The right aromatic ring is substituted with a group  $R_{10}$  and a side chain  $-C(=Y_5)-[C(R_7)(R_8)]_s-[C(R_5)(R_6)]_t-$ . The central chain consists of two repeating units:  $-O-C(=Y_6)-[C(L_2)]_r-$  and  $-R_2-L_2-[C(Y_6)]_q-$ .


$$V_a - \text{C}(=\text{O})\text{CH}_2\text{N}(\text{OAc})\text{CH}_2\text{O}\text{C}(=\text{O})\text{CH}_2\text{OC}(=\text{O})\text{CH}_2\text{OCH}_2\text{CH}_2\text{NH}\text{C}(=\text{O})\text{OCH}_2\text{R}_1\text{OCH}_2\text{C}(=\text{O})\text{NH}\text{CH}_2\text{CH}_2\text{OC}(=\text{O})\text{CH}_2\text{OC(=O)CH}_2\text{OCH}_2\text{N}(\text{OAc})\text{CH}_2\text{C(=O)V}$$

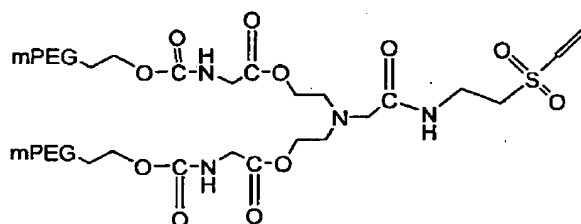
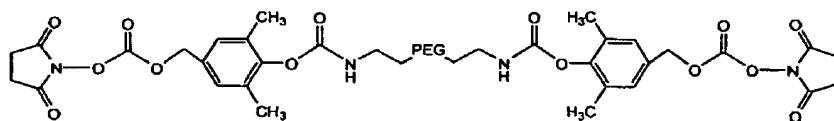
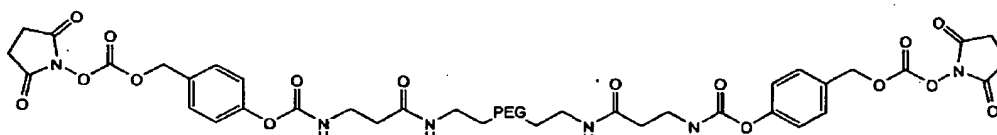
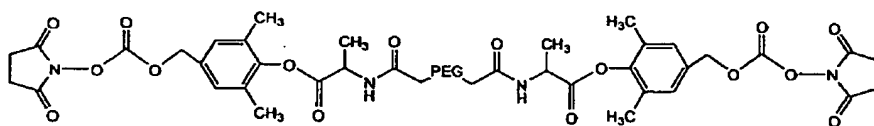
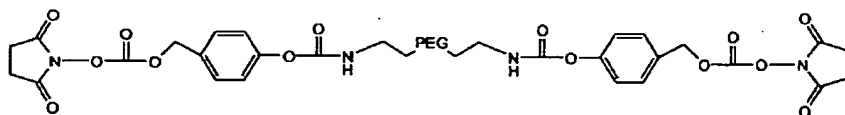
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wherein  $V_a$  is

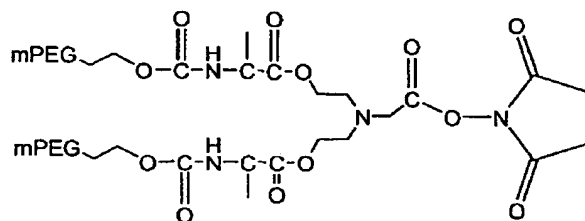
7. (Original) The method of claim 1, wherein said polymer containing said leaving group is selected from the group consisting of



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and

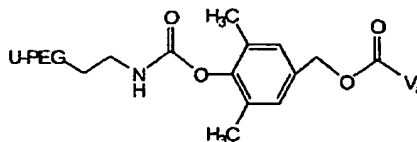
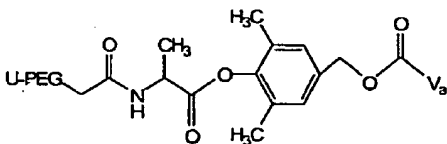
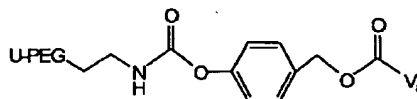
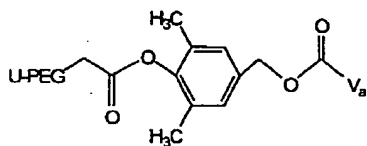
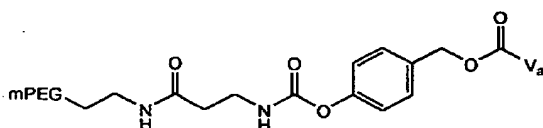
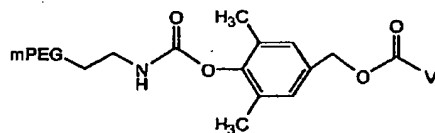
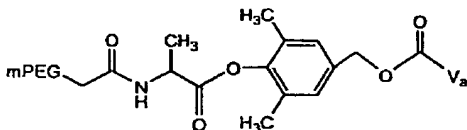
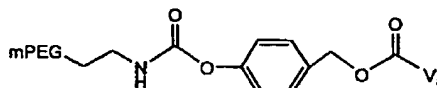
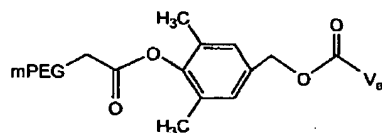


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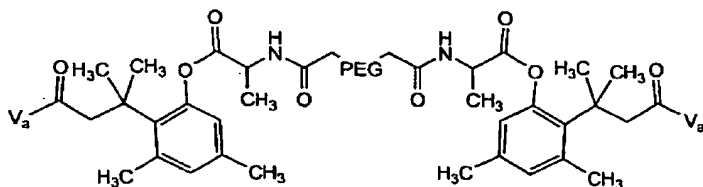
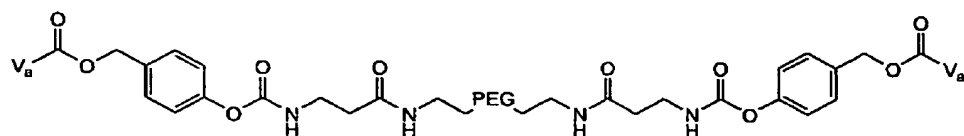
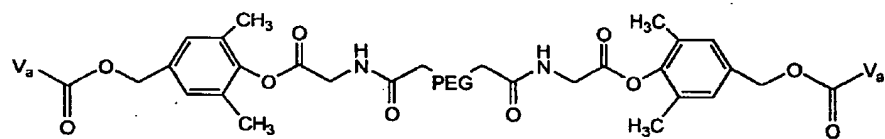
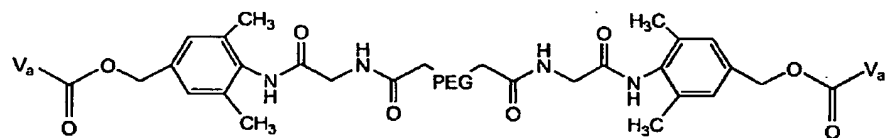
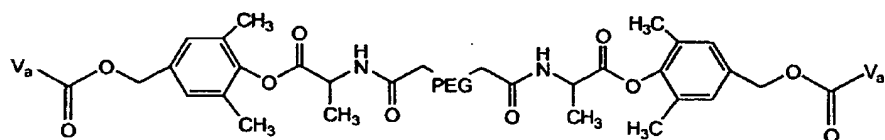
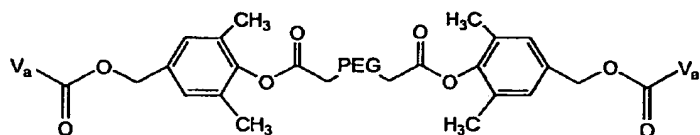
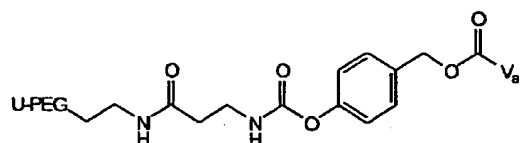
8. (Original) The method of claim 2, wherein  $R_1$  and  $R_2$  are independently selected polyalkylene oxide residues and  $R'_1$  and  $R'_2$  are independently selected branched polyalkylene oxide residues.

9. (Original) The method of claim 2, wherein  $R_1$  and  $R_2$  are independently selected polyethylene glycol residues and  $R'_1$  and  $R'_2$  are independently selected branched polyethylene glycol residues.

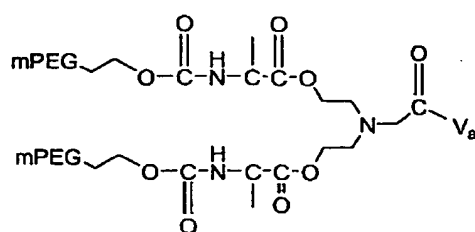
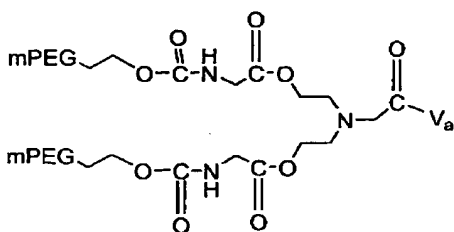
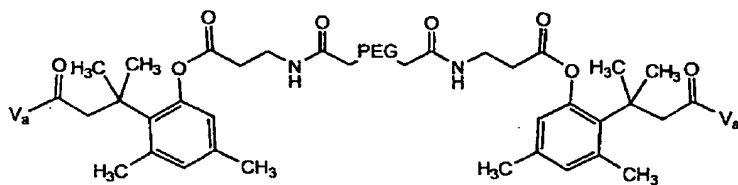
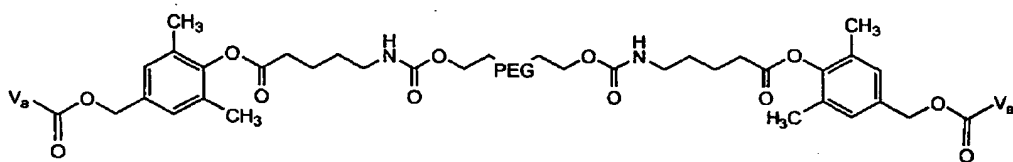
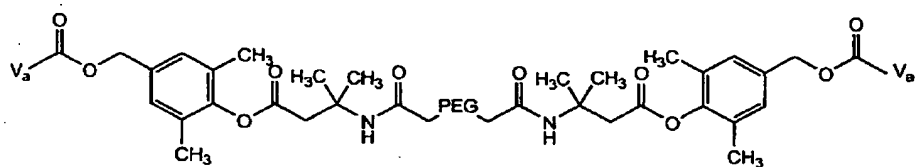
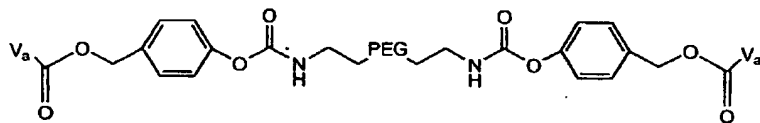
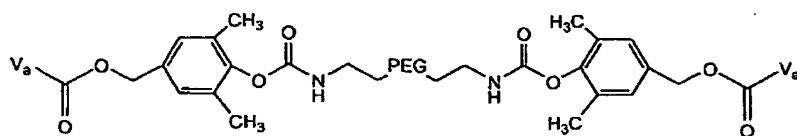
10. (Original) The method of claim 1, wherein said vancomycin-polymer conjugate is selected from the group consisting of



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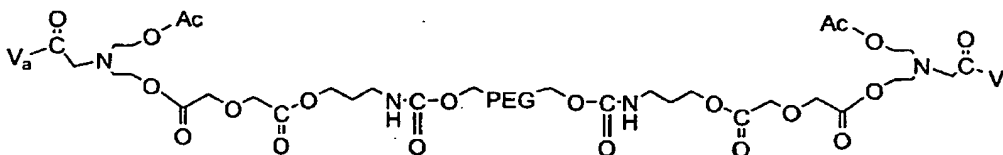


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and

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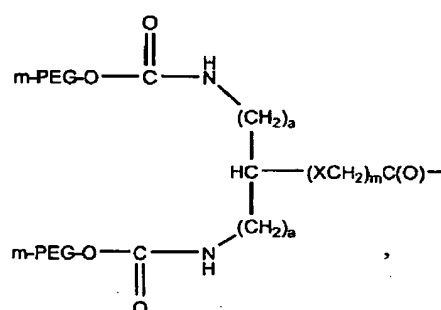
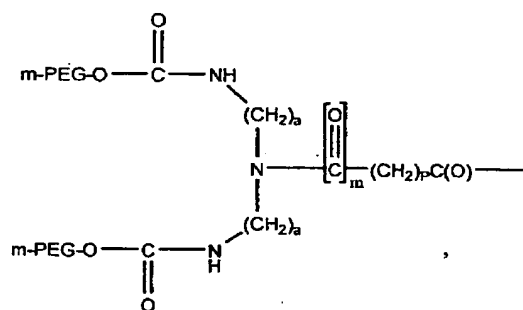
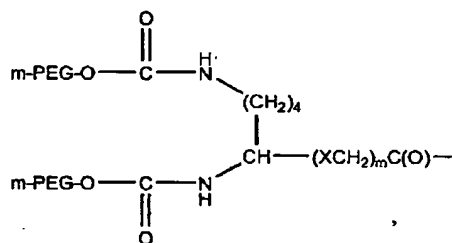
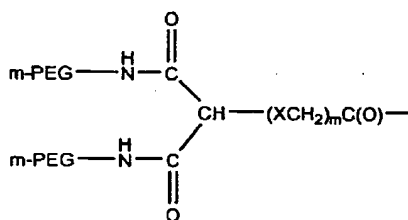
wherein

PEG is  $-\text{O}(\text{CH}_2\text{CH}_2\text{O})_x-$ ;

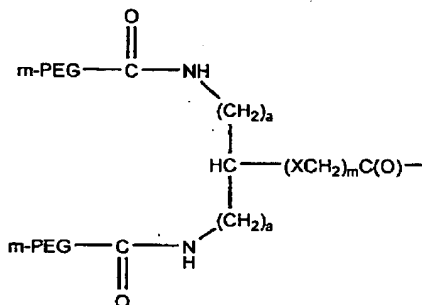
mPEG is  $\text{H}_3\text{CO}(\text{CH}_2\text{CH}_2\text{O})_x-$ ;

x is a positive integer selected from about 10 to about 2300, and

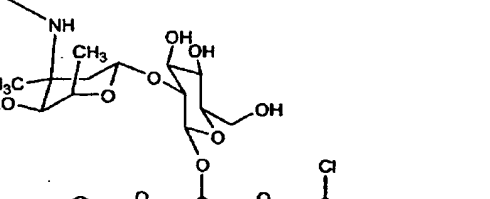
U-PEG is selected from the group consisting of



and

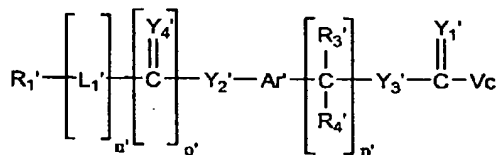


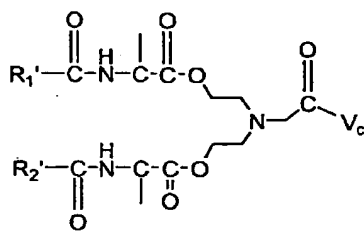
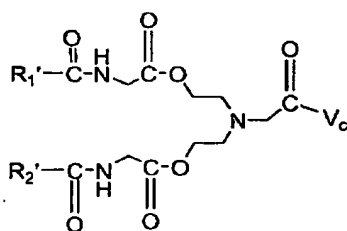
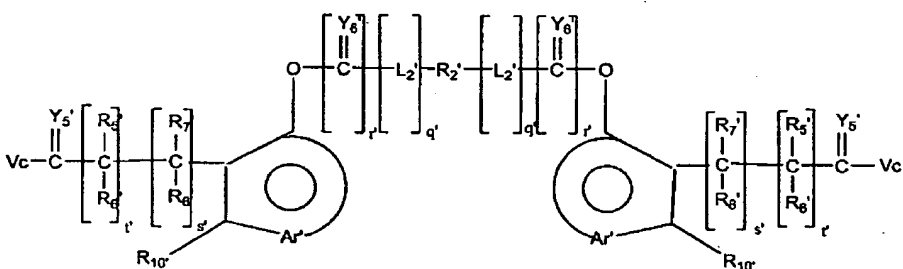
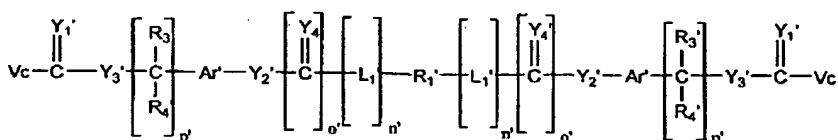
V<sub>a</sub> is



Chemical structure of V<sub>a</sub> is shown, which is a complex molecule featuring a central chain of amide and ester linkages, substituted with various aromatic and aliphatic groups, including a chlorophenyl ring, a 4-hydroxyphenyl ring, and a 2,4,6-trihydroxyphenyl ring. The structure also includes a methyl group, a hydroxyl group, and a carboxylic acid group.

12. (Original) The method of claim 10, wherein said vancomycin-polymer conjugate containing said polymer residue attached on both of said sugar amino group and said N-methyl amino group is selected from the group consisting of:

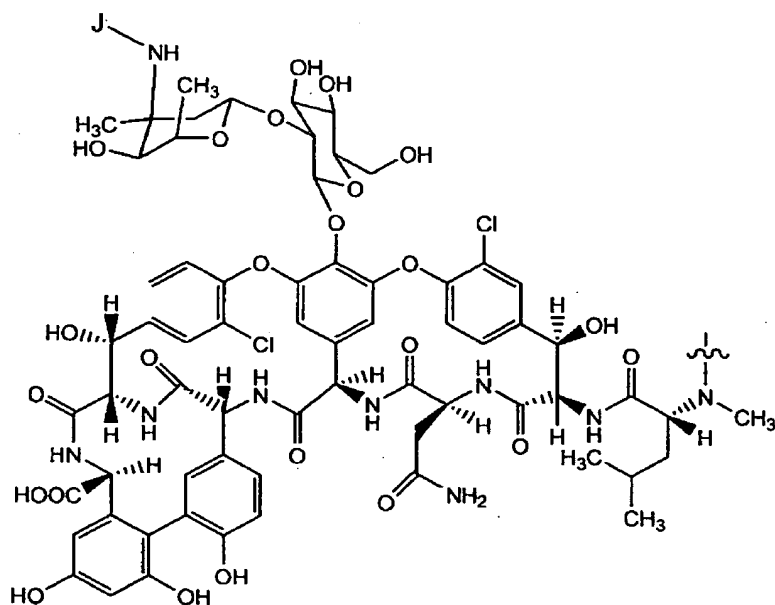


[illegible]
$$\text{V}_c - \text{C}(=\text{O}) - \text{CH}_2 - \text{N}(\text{OAc}) - \text{CH}_2 - \text{O} - \text{C}(=\text{O}) - \text{CH}_2 - \text{O} - \text{C}(=\text{O}) - \text{CH}_2 - \text{O} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{NH} - \text{C}(=\text{O}) - \text{O} - \text{CH}_2 - \text{R}_1 - \text{CH}_2 - \text{O} - \text{C}(=\text{O}) - \text{NH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{O} - \text{C}(=\text{O}) - \text{CH}_2 - \text{O} - \text{C}(=\text{O}) - \text{O} - \text{CH}_2 - \text{N}(\text{OAc}) - \text{C}(=\text{O}) - \text{V}_c$$

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wherein

Vc is:



wherein:

J is H or a polymer residue containing a capping group,

R<sub>1</sub>' and R<sub>2</sub>' are independently selected polymeric residues;Y<sub>1-6</sub>' are independently selected from the group consisting of O, S or NR<sub>9</sub>';

R<sub>3-10</sub>' are the same or different and are each independently selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyls, C<sub>3-12</sub> branched alkyls, C<sub>3-8</sub> cycloalkyls, C<sub>1-6</sub> substituted alkyls, C<sub>3-8</sub> substituted cycloalkyls, aryls, substituted aryls, aralkyls, C<sub>1-6</sub> heteroalkyls, substituted C<sub>1-6</sub> heteroalkyls, C<sub>1-6</sub> alkoxys, phenoxys and C<sub>1-6</sub> heteroalkoxys;

Ar' is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

L<sub>1</sub>' and L<sub>2</sub>' are independently selected bifunctional linkers;

p' and t' are independently selected positive integers;

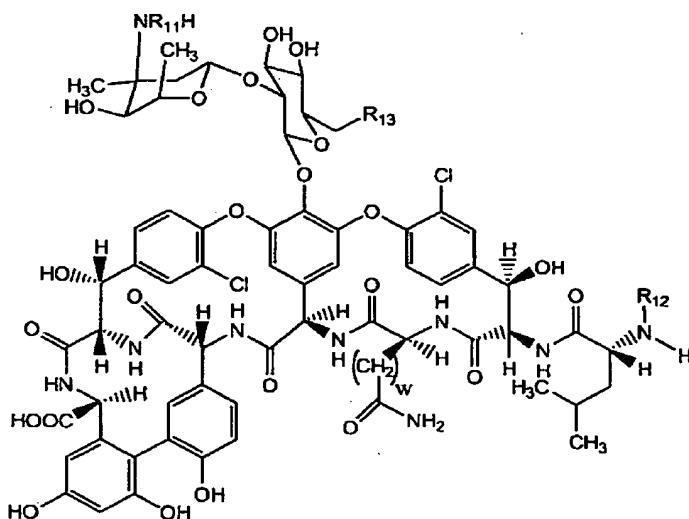
n', q' and s' are independently either zero or a positive integer;

o' and r' are independently zero or one; and

all other variables are as previously defined.

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13. (Original) The method of claim 10, wherein said solvent mixture comprises about equal parts dichloromethane and dichloroformamide.
14. (Original) The product prepared by the method of claim 1.
15. (Original) The product prepared by the method of claim 10.
16. (Original) The method of claim 1, wherein said molar excess of triethylamine is at least about 30-fold.
17. (Original) A method of preparing a vancomycin-polymer conjugate wherein said conjugate has a polymer residue attached on both the sugar amino and the N-methyl amino of said vancomycin compound, comprising: reacting a vancomycin compound of the formula:



wherein

$R_{11}$  and  $R_{12}$  are each independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  hetero-alkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxyalkyl, phenoxyalkyl, and  $C_{1-6}$  heteroalkoxys;

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$R_{13}$  is OH, NH-aryl, NH-aralkyls, NH-alkyl-aryl or NH- $C_{1-12}$  alkyl; and

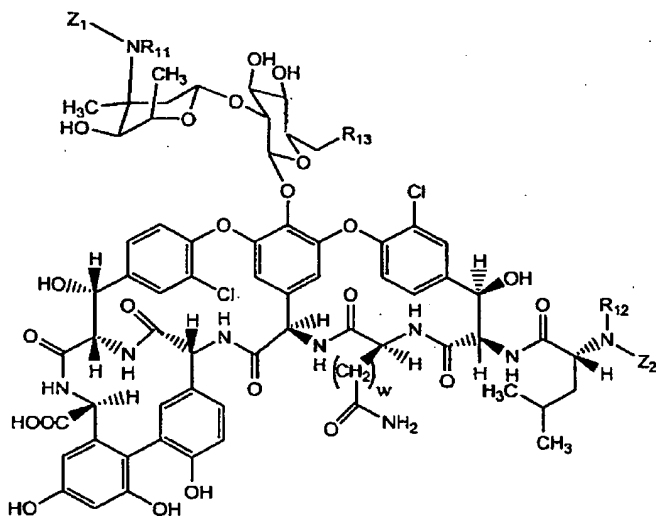
w is 1 or 2;

with at least about 2 equivalents of a polymer residue containing at least one leaving group capable of reacting with the sugar amino group and the N-methyl amino group of said vancomycin compound in the presence of at least about a five-fold molar excess of dimethylaminopyridine (DMAP) and a sufficient amount of a solvent mixture comprising dichloromethane (DCM) and dimethyl formamide (DMF).

18. (Original) The method of claim 17, wherein said solvent mixture comprises about equal parts dichloromethane and dichloroformamide.

19. (Original) The product prepared by the method of claim 17.

20. (Currently Amended) The product prepared by the method of claim 19, wherein said vancomycin-polymer conjugate comprises the formula:



wherein:

$R_{11}$  and  $R_{12}$  are independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  heteroalkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxyalkyl,

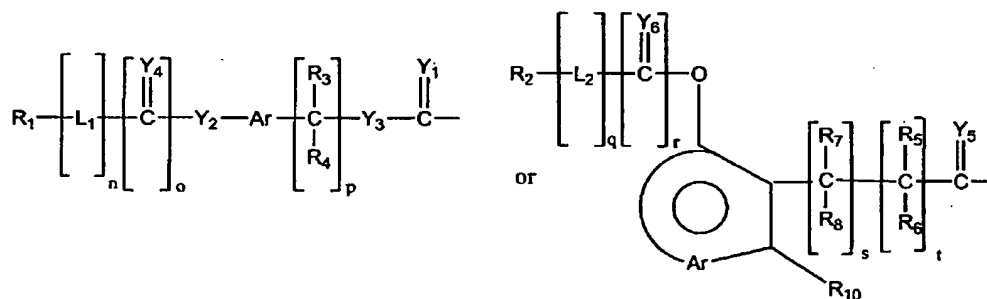
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phenoxyalkyl and C<sub>1-6</sub> heteroalkoxys;

R<sub>13</sub> is OH, NH-aryl, NH-aralkyls, or NH-C<sub>1-12</sub> alkyl; and

w is 1 or 2;

Z<sub>1</sub> and Z<sub>2</sub> are



wherein

R<sub>1</sub> and R<sub>2</sub> are independently selected polymeric residues;

Y<sub>1-6</sub> are independently selected from the group consisting of O, S or NR<sub>9</sub>;

R<sub>3-10</sub> are independently selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyls, C<sub>3-12</sub> branched alkyls, C<sub>3-8</sub> cycloalkyls, C<sub>1-6</sub> substituted alkyls, C<sub>3-8</sub> substituted cycloalkyls, aryls, substituted aryls, aralkyls, C<sub>1-6</sub> heteroalkyls, substituted C<sub>1-6</sub> heteroalkyls, C<sub>1-6</sub> alkoxy, phenoxy and C<sub>1-6</sub> heteroalkoxy;

Ar is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

L<sub>1</sub> and L<sub>2</sub> are independently selected bifunctional linkers;

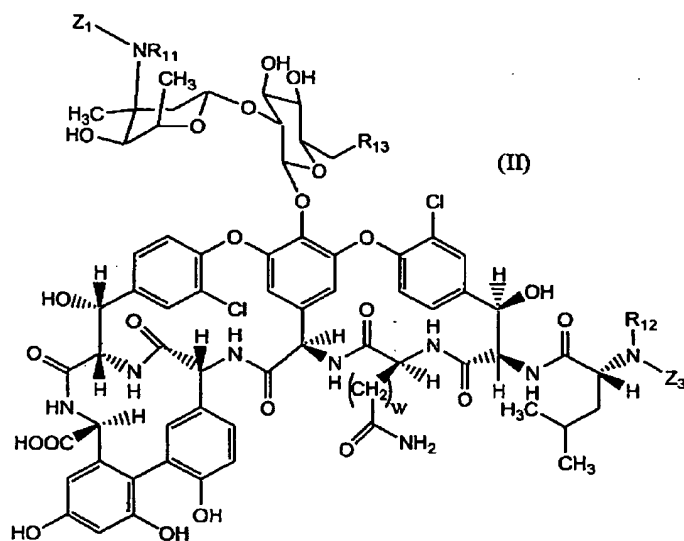
p and t are independently selected positive integers;

n, q and s are independently either zero or a positive integer; and

o and r are independently zero or one.

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21. (Original) A vancomycin polymer conjugate comprising the formula:



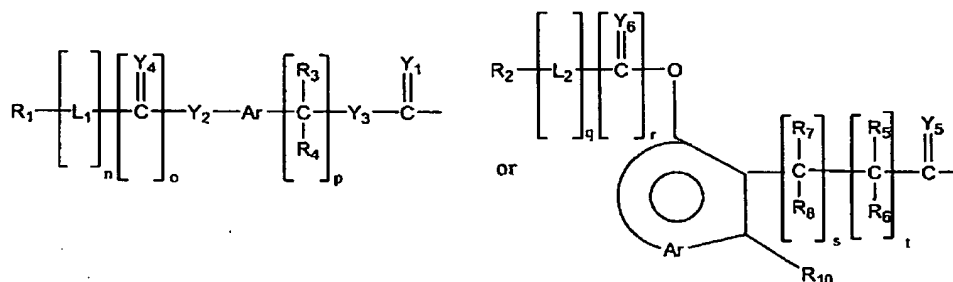
wherein:

$R_{11}$  and  $R_{12}$  are each independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  heteroalkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxyalkyl, phenoxyalkyl, and  $C_{1-6}$  heteroalkoxys;

$R_{13}$  is OH, NH-aryl, NH-aralkyls, or NH- $C_{1-12}$  alkyl;

w is 1 or 2; and

$Z_1$  is



wherein

$R_1$  and  $R_2$  are independently selected polymeric residues;

$Y_{1-6}$  are independently selected from the group consisting of O, S or  $NR_9$ ;

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$R_{3-10}$  are the same or different and are each independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  heteroalkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxy, phenoxy and  $C_{1-6}$  heteroalkoxy;

Ar is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

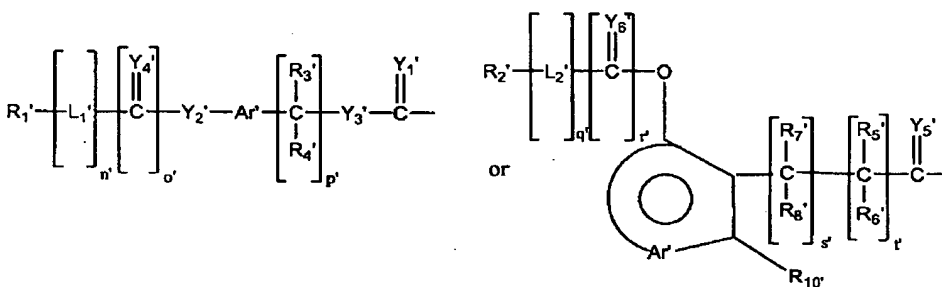
$L_1$  and  $L_2$  are independently selected bifunctional linkers;

p and t are independently selected positive integers;

n, q and s are independently either zero or a positive integer; and

o and r are independently zero or one; and

$Z_3$  is



wherein

$R_1'$  and  $R_2'$  are independently selected polymeric residues;

$Y_{1-6}'$  are independently selected from the group consisting of O, S or  $NR_9'$ ;

$R_{3-10}'$  are the same or different and are each independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  heteroalkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxy, phenoxy and  $C_{1-6}$  heteroalkoxy;

Ar' is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

$L_1'$  and  $L_2'$  are independently selected bifunctional linkers;

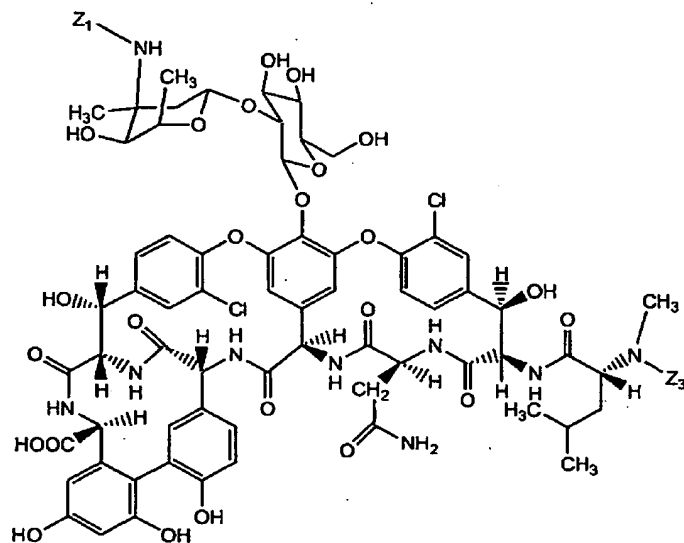
p' and t' are independently selected positive integers;

n', q' and s' are independently either zero or a positive integer; and

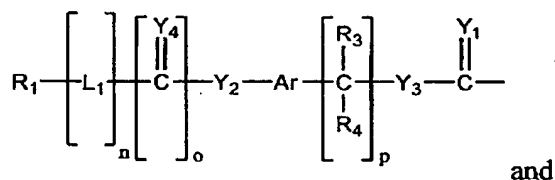
o' and r' are independently zero or one.

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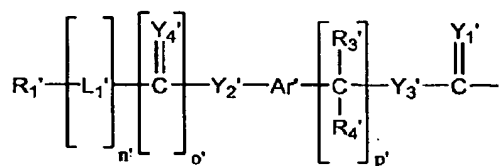
22. (Original) A vancomycin polymer conjugate of claim 21, comprising the formula



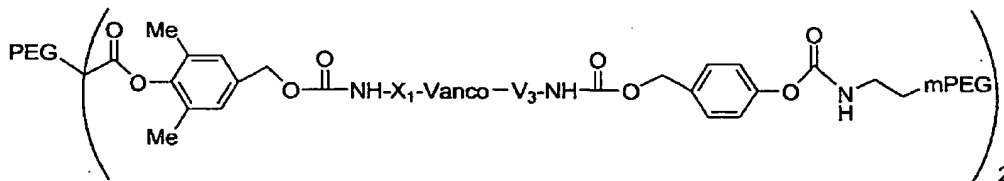
23. (Original) The vancomycin polymer conjugate of claim 22, wherein  $Z_1$  is



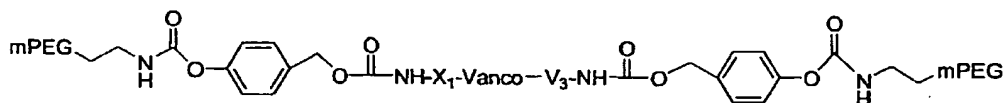
$Z_3$  is



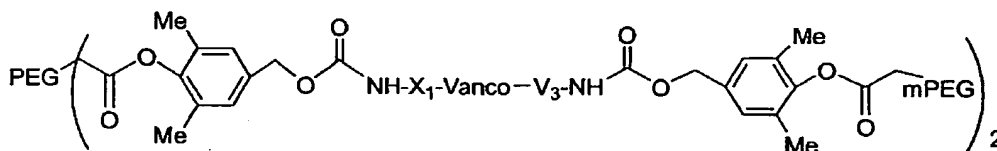
24. (Original) A vancomycin polymer conjugate of claim 21, selected from the group consisting of:



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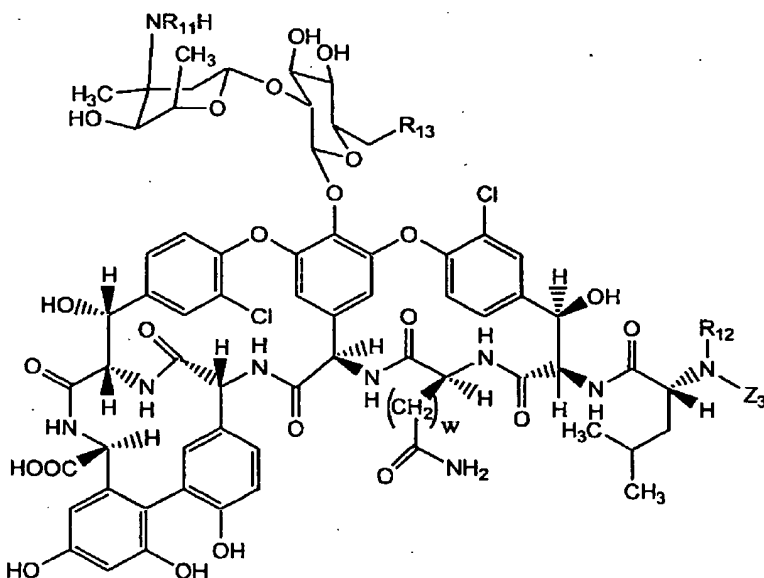
and



25. (Original) The polymer conjugate of claim 21, wherein  $Y_{1-4}$  and  $Y_{1-4}'$  are each O.
26. (Original) The polymer conjugate of claim 21, wherein  $R_{3-8}$  and  $R_{3-8}'$  are independently selected from the group consisting of hydrogen, methyl and ethyl; and p, p', t and t' are each one.
27. (Original) The polymer conjugate of claim 21, wherein  $R_1$ ,  $R_1'$ ,  $R_2$  and  $R_2'$  are independently selected polyalkylene oxide residues.
28. (Original) The polymer conjugate of claim 21, wherein  $R_1$ ,  $R_1'$ ,  $R_2$  and  $R_2'$  are independently selected polyethylene glycol residues.
29. (Original) The polymer conjugate of claim 27, wherein said polyalkylene oxide has a weight average molecular weight of from about 2,000 Da to about 100,000 Da.

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30. (Original) A vancomycin-polymer conjugate comprising the formula:



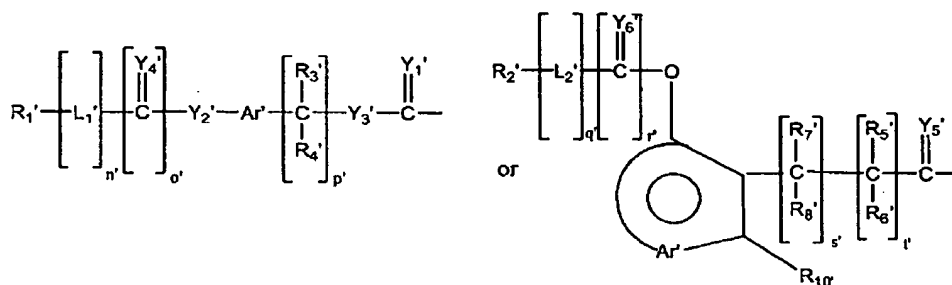
wherein

$R_{11}$  and  $R_{12}$  are independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  heteroalkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxyalkyl, phenoxyalkyl, and  $C_{1-6}$  heteroalkoxys;

$R_{13}$  is OH, NH-aryl, NH-aralkyl, or NH- $C_{1-12}$  alkyl; and

$w$  is 1 or 2;

$Z_3$  is



wherein

$R_1'$  and  $R_2'$  are independently selected polymeric residues;

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$Y_{1-6}'$  are independently selected from the group consisting of O, S or  $NR_9'$ ;

$R_{3-10}'$  are the same or different and are each independently selected from the group consisting of hydrogen,  $C_{1-6}$  alkyls,  $C_{3-12}$  branched alkyls,  $C_{3-8}$  cycloalkyls,  $C_{1-6}$  substituted alkyls,  $C_{3-8}$  substituted cycloalkyls, aryls, substituted aryls, aralkyls,  $C_{1-6}$  heteroalkyls, substituted  $C_{1-6}$  heteroalkyls,  $C_{1-6}$  alkoxys, phenoxys and  $C_{1-6}$  heteroalkoxys;

$Ar'$  is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

$L_1'$  and  $L_2'$  are independently selected bifunctional linkers;

$p'$  and  $t'$  are independently selected positive integers;

$n'$ ,  $q'$  and  $s'$  are independently either zero or a positive integer; and

$o'$  and  $r'$  are independently zero or one.

31. (Original) A method of treatment, comprising administering an effective amount of a compound of claim 21.

32. (Currently Amended) A method of treating a vancomycin susceptible disease in a mammal comprising administering an effective amount of a compound of claim 10  $\pm$ , to a mammal in need of such treatment, whereby, the compound of claim 10  $\pm$  undergoes degradation and releases vancomycin or a vancomycin derivative *in vivo*.

33. (Original) A method of treating a vancomycin susceptible disease in a mammal comprising administering an effective amount of a compound of claim 21, to a mammal in need of such treatment, whereby, the compound of claim 21 undergoes degradation and releases vancomycin or a vancomycin derivative *in vivo*.

34. (Currently Amended) A method of treating a vancomycin susceptible disease in a mammal comprising administering to a mammal in need of such treatment, an effective amount of a combination of vancomycin or a pharmaceutically acceptable salt, solvate or hydrate thereof, and a compound of claim 10  $\pm$ , wherein said vancomycin and said compound of claim 10  $\pm$  are administered either substantially concurrently in separate dosage forms or combined in a unit dosage form.

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35. (Currently Amended) A kit comprising in separate containers in a single package, pharmaceutical compositions for use in combination to treat a vancomycin susceptible disease which comprises in one container a therapeutically effective amount of vancomycin or a pharmaceutically acceptable salt, solvate or hydrate thereof in a pharmaceutically acceptable carrier and in a second container a therapeutically effective amount of a compound of claim 10 or a pharmaceutically acceptable salt, solvate or hydrate thereof in a pharmaceutically acceptable carrier.